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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/486,070 06/07/95 STAVRIANOPOULOS

18N1/1002

RONALD C FEDUS  
ENZO DIAGNOSTICS INC  
ENZO BIOCHEM INC  
575 FIFTH AVENUE 18TH FLOOR  
NEW YORK, NY 10017

MARSCHEL, A

EXAMINER

ART UNIT	PAPER NUMBER
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1807

22

10/02/95

DATE MAILED:

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS☒ This application has been examined ☒ Responsive to communication filed on 6-7-95 ☐ This action is made final.A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

- |   |   |
|---|---|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892.        | 2. <input type="checkbox"/> Notice of Draftsman's Patent Drawing Review, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449.             | 4. <input type="checkbox"/> Notice of Informal Patent Application, PTO-152.       |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/>   |

**Part II SUMMARY OF ACTION**1. ☒ Claims 27-47 are pending in the application.

Of the above, claims \_\_\_\_\_ are withdrawn from consideration.

2. ☒ Claims 1-26 have been cancelled.3. ☐ Claims \_\_\_\_\_ are allowed.4. ☒ Claims 27-47 are rejected.5. ☐ Claims \_\_\_\_\_ are objected to.6. ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.8. ☐ Formal drawings are required in response to this Office action.9. ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).11. ☐ The proposed drawing correction, filed \_\_\_\_\_, has been ☐ approved; ☐ disapproved (see explanation).12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received  
☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.14. ☐ Other

EXAMINER'S ACTION

AM  
PTOL-328 (Rev. 2/93)  
08/486,070

Applicants' arguments; filed 9/2/94 as the last response in the parent, serial number 07/967,646; have been fully considered and they are deemed to be persuasive to overcome the rejections set forth in the previous office action, mailed 7/25/94.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Due to the withdrawal of the previously applied rejections, the finality of the office action, mailed 7/25/94, was withdrawn.

The proposed amendments, filed as after final amendments on 9/2/94 and 10/28/94, were both denied entry because both proposed amendments contain NEW MATTER as discussed in the office action, mailed 1/5/95 in the parent serial number 07/967,646. Neither of these amendments have been entered because applicants' request for a file-wrapper-continuation did not contain a request to enter either amendment and they were denied entry when their status was of after final amendments.

If applicant desires priority under 35 U.S.C. § 120 based upon a parent application, specific reference to the parent application must be made in the instant application. It is noted that this appears as the first sentence of the specification following the title, preferably as a separate paragraph. Status of the parent application (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "Patent No." should follow the filing date of the parent application. If a parent application has become abandoned, the expression "abandoned" should follow the filing date of the parent application.

The above paragraph is appropriate because in the cross reference to other related applns the app # 07/607,347 should

have been listed as having been abandoned.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the disclosure, as originally filed, does not provide support for the invention as is now claimed.

The preliminary amendment, filed 10/28/92, has been filed in a continuation application and therefore any added disclosure therein is NEW MATTER compared to the earlier filed application of which the instant one is also a continuation. Claim 27 contains NEW MATTER in that a composition is therein cited without "composition" being defined or given in a written description as filed. It is noted that various probes are cited on page 9 in the first paragraph of the SUMMARY OF THE INVENTION but not compositions such as a mixture containing said probe or probes. Additionally, the claimed composition is cited in claim 27 as comprising a system discussed above as containing NEW MATTER and wherein such a "system" also lacks written basis as filed. Also, comparing claims 24-26 as filed to claim 27, it is clear that a solid support with a polynucleotide with or without a hybridized and chemically labeled polynucleotide or oligonucleotide probe is the scope of the instant invention and

not a composition "comprising" a "system" which further comprises a double-stranded oligonucleotide or polynucleotide. These three layers of subject matter go far beyond claim 24, for example, as filed, and therefore are deemed to contain NEW MATTER. Also claims 27 and 28 contain NEW MATTER similar to non-entered claims 48 and 49 as discussed above regarding a solid support subelement in a system as submitted but not entered in the parent application. The "same" or "different" limitations of claims 34 and 35 have not been found as filed as also the sandwich type formats of claims 36 and 37. Similarly, the limitation directed to direct or indirect attachment of signalling moiety to the chemical label of claim 42 is NEW MATTER as being a separate limitation from that of claim 41. The apparatus of claim 46 is not limited to a "plurality of devices" as are all of the apparatus disclosures as filed. In summary, the preliminary amendment filed 10/28/92 contains many NEW MATTER disclosures in claims 27-47 that are have no written description in the instant application as filed.

Claims 27-47 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the above objection to the specification.

Claims 31-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is unclear in that what appears to be a Markush

group lists plastic as well as polystyrene, dextran, and polypropylene because polystyrene, dextran, and polypropylene are plastics. What are the metes and bounds of the claim unless it is merely inclusive of any plastic?

Claims 32 and 33 are vague and indefinite in that the cooperativity between the members listed therein and the solid support of the "system" is not defined. Seemingly the cited members of claims 32 and 33 are meant to be options for the solid support of claim 27 but this is not clearly defined as such. Could applicants mean the solid support and the members to be separate components of the claimed "system"? Clarification is requested as to the metes and bounds and relationships of the components of the claimed "system".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 27-31, 34-36, 38, 39, and 41-45 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Stuart et al.

Stuart et al. disclose the formation of DNA-RNA hybrids by

in situ hybridization performed on microscope slides wherein the hybrids are detected by antibody binding to said hybrids starting in column 4, line 1, and proceeding through the section entitled "EXPERIMENTAL". Several types of antibody label types are given in Stuart et al. in column 4, lines 37-55, inclusive of enzymes such as horseradish peroxidase. These disclosures read on the above listed instant claims. It is additionally noted that microscope slides are non-porous and transparent and are disclosed as being viewed by light microscopy as summarized in column 6, lines 17-26, thus also inclusive of a "system" as instantly claimed. Such a light microscope system includes non-porous transparent elements which are interpretable as reading on these limitations of the system of the instant claims. It is also noted that Stuart et al. reads on the above listed instant claims after removal of the NEW MATTER discussed above. The above listed claims contain the limitation directed to "a signalling moiety which is capable of generating a soluble signal". Enzymes such as horseradish peroxidase inherently are "capable of generating a soluble signal" as is well known in the peroxidase labeled antibody art. It is acknowledged that Stuart et al. does not disclose the actual generation of a soluble signal. This lack of actual soluble signal generation is, however, not deemed to prevent this rejection because the claims are composition claims citing only the "capability" of generating such a soluble signal. The inherency of this "capability" has been discussed above.

Claims 27-31, 34-36, 38, 39, and 41-45 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated either by Langer-Safer et al. or Manuelidis et al.

The listed claims are anticipated either by Langer-Safer et al. or Manuelidis et al. in the same manner as the above rejection based on Stuart et al. because both references also discussed the performance of in situ hybridization of chromosome spreads on microscope slides etc. as summarized above. It is noted that Langer-Safer et al. has been listed on a PTO Form 1449, filed by applicants on 6/2/94, as Langer et al. (1982) as given in PNAS, volume 79, pages 4381-4385. The correct citation is to Langer-Safer et al. and has also been corrected on the PTO Form 1449.

Claims 27-31, 34-36, and 38-45 are rejected under 35 U.S.C. § 102(e) as being anticipated by Ward et al.

Ward et al. disclose via the "GENERAL PROTOCOL" and with connected discussion elsewhere at the bottom of columns 19 and 20 in situ hybridization where immobilized double-stranded nucleic acid is shown visualized with a biotinylated probe bound to avidin-peroxidase. This reads on the listed claims as does the above disclosures directed to in situ hybridization but also covering biotin-avidin mediated embodiments.

Claims 32, 33, 37, 46, and 47 are allowable over the prior art of record because the prior art of record does not teach or suggest the well, tube, or cuvette practice as solid supports for enzyme labeled hybridization nor sandwich hybridization used for

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immobilizing a probe/target hybrid. A terminal disclaimer has been filed over Patent Number 4,994,373 to overcome and prevent any obviousness-type double patenting rejections.

Applicants are hereby informed that the prior art made of record as having been considered in the parent application serial number 07/967,646 is also hereby made of record in the instant application as having been considered.

No claim is allowed.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

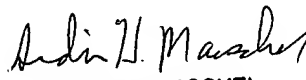
The CM1 Fax Center number is either (703) 305-3014 or (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

September 29, 1995

  
ARDIN H. MARSCHEL  
PATENT EXAMINER  
GROUP 1800